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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/017,715	02/03/98	JI H	1488.0810003

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EXAMINER	
CANELLA,K	
ART UNIT	**PAPER NUMBER**
1642	17

DATE MAILED: 11/22/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/017,715	Ji et al
Examiner	**Group Art Unit**
Karen Canella	1642

☐ Responsive to communication(s) filed on _____

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3 months* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *16-79* is/are pending in the applicat

Of the above, claim(s) *79* is/are withdrawn from consideration

☒ Claim(s) *17 and 19* is/are allowed.

☒ Claim(s) *16, 18, and 20-78* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

Response to Arguments

1. Please note that the examiner assigned to your application in the PTO has changed.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Claims 16-78 are under consideration.

4. Applicant argues that the examiner has erred in refusing rejoinder of claim 79 with claims 16-78. Applicant has put forth M.P.E.P. 803.04 to argue that although ten nucleotide sequences encoding different proteins are distinct and ordinarily would be subject to a restriction requirement, up to ten nucleotide sequences encoding different proteins should be examined together in one application due to the partial wavier of the requirements of 37 CRF 1.141. Applicant concludes that the invention of claim 79, reading on SEQ ID NO:12, should be rejoined with the instant claims drawn to SEQ ID NO:1. This is not found persuasive. As discussed further in M.P.E.P. 803.04, the partial wavier of the requirements of 37 CRF 1.141 is to be applied to DNA fragments comprising DNA having at least 95% homology to a single SEQ ID NO, and a combination of DNA fragments comprising a single SEQ ID NO. Further, SEQ ID NO:1, consisting of 550 bases, and SEQ ID NO:12, consisting of 755 bases, represent complete open reading frames of distinct genes and therefore SEQ ID NO:1 and 12 cannot be considered a "fragments" of a larger SEQ ID NO, but as separate polynucleotides.

5. The rejection of claims 16-22, 24-28, 30-34, 36-40, 42-48, 50-54, 56-62, and 64-68 under 35 U.S.C. 101 because the claimed invention is not supported by either a specific substantial and credible utility or a well-established utility is withdrawn.

6. The rejection of claims 23, 29, 35, 41, 49, 55, 63 and 69 under 35 U.S.C. 101 because the claimed invention is not supported by either a specific substantial and credible utility or a well-established utility is maintained for reasons of record. Applicant argues that SEQ ID NO:2, the putative polynucleotide encoded by SEQ ID NO:1, would be useful in the production of BCSG1 specific antibodies, and thus useful for the diagnosis and treatment of breast cancer. This is not found persuasive. There is no evidence in the specification nor any art of record to document that SEQ ID NO:1 is translated into a peptide which is expressed or overexpressed in malignant breast tissue. It is well known in the art that the process of translation of mRNA into protein, vs. degradation of the mRNA without translation is conrolled by many mechanisms within the cell (for example see: Molecular Biology of the Cell (textbook), Bruce Alberts, Ed., third edition, pg. 40). Therefore, one of skill in the art would not be able to predict if SEQ ID NO:1 was in fact translated into the polypeptide of SEQ ID NO:2. The specification gives only general suggestions regarding the production of antibodies which could be applied to many different proteins and peptides. Thus the asserted utility for hypothetical SEQ ID NO:2 is a general utility, not specific to SEQ ID NO:1. The teachings in the specification are an invitation to experiment wherein the artisan is invited to elaborate a functional use for a putative polypeptide. Because the claimed invention is not supported by a specific asserted utility for the reasons set forth, credibility of any utility cannot be assessed.

7. Claims 23, 29, 35, 41, 49, 55, 63 and 69 are rejected under 35 U.S.C. 112, first paragraph for reasons of record. Specifically, since the claimed invention is not supported by a substantial, specific and credible utility or a well established utility for the reasons set forth in the rejection under 35 USC 101 above, one skilled in the art clearly would not know how to use the claimed invention.

43-56, 78 71-77 95%

8. Claims 16, 18, 20-22, 24-28, 30-34, 36-40, 42-48, 50-54, 56-62, 64-68 and 70-78 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for SEQ ID NO:1, does not reasonably provide enablement for isolated polynucleotides encoding SEQ ID NO:2 or isolated polynucleotides encoding the complete amino acid sequence encoded by the cDNA of the ATCC clone 97856, or isolated polynucleotides comprising fragments of SEQ ID NO:1 further comprising heterologous polynucleotides, or polynucleotides encoding fragments of SEQ ID NO:2 further comprising heterologous polynucleotides; polynucleotides having 95% identity to polynucleotides which encode SEQ ID NO:2; isolated polynucleotides encoding variants of SEQ ID NO:2, said variants having one to thirty conservative amino acids substitutions with respect to SEQ ID NO:2; isolated polynucleotides having 95% identity to SEQ ID NO:1; and isolated polynucleotides which hybridize to SEQ ID NO:1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

(A)As drawn to polynucleotides encoding the complete amino acid sequence encoded by the cDNA of the ATCC clone 97856 polynucleotides encoding SEQ ID NO:2, polynucleotides comprising nucleic acids which encode for fragments of SEQ ID NO:2, and polynucleotides comprising fragments of the polynucleotide encoding SEQ ID NO:2, said polynucleotides further comprising undisclosed polynucleotides.

Claims 16, 18, 20-22, 24-28, 30-34, 36- 40, 42, 57-61, 64-68 and 70 are drawn to polynucleotides encoding SEQ ID NO:2, polynucleotides encoding fragments of SEQ ID NO:2, and polynucleotides comprising nucleic acids which encode for fragments of SEQ ID NO:2 said polynucleotides further comprising heterologous polynucleotides. The specification has not demonstrated that the protein of SEQ ID NO:2 is translated (see paragraph 6, supra) nor has it taught a specific use of the hypothetical SEQ ID NO:2, and further, the specification does not teach a polynucleotide which encodes a large fragment of SEQ ID NO:2 which further comprises a heterologous polynucleotide. Specifically, since the specification is not enabling for SEQ ID

NO:2 for the reasons put forth in paragraph 5, supra, it is not enabling for polynucleotides encoding SEQ ID NO:2, or polynucleotides comprising nucleic acids which encode fragments of SEQ ID NO:2.

(B)As drawn to polynucleotides comprising fragments of SEQ ID NO:1, and polynucleotides comprising fragments of SEQ ID NO:1, wherein said polynucleotides further comprise undisclosed polynucleotides.

Claims 43-48, 50-54 and 56 are broadly drawn to polynucleotides comprising 50 or 100 or 250 contiguous nucleotides of SEQ ID NO:1 which further comprise undisclosed polynucleotides. There is no limitations in the claims or the specification regarding these polynucleotide variants of SEQ ID NO:1. The specification does not teach a heterologous polynucleotide comprising any fragments of SEQ ID NO:1 The specification teaches that the full polynucleotide sequence of SEQ ID NO:1 is a useful marker for breast cancer progression. The specification further discloses on pg 49, line 23, the BCSG1 probe as a 550 bp full-length cDNA (SEQ ID NO:1). The specification does not teach a use for polypeptides comprising 50, 100 or 250 contiguous nucleotides of SEQ ID NO:1 which further comprise heterologous polynucleotides, since the specification puts forth only full-length SEQ ID NO:1 as a probe. Given the lack of guidance in the specification, one of skill in the art would be forced into undue experimentation in order to use the claimed polynucleotides which comprise undisclosed heterologous polynucleotides.

(C)As drawn to polynucleotides 95% identical to polynucleotides encoding SEQ ID NO:2 and polynucleotides encoding variants of SEQ ID NO:2.

Claims 71 and 76 are drawn to polynucleotides which are 95% identical to the polynucleotides which encode SEQ ID NO:2. Claims 72-75 are drawn to a polynucleotide which encode variants of SEQ ID NO:2, said variants having from one to thirty conservative amino acid substitutions with respect to the amino acid sequence of SEQ ID NO:2. The specification is not enabling for SEQ ID NO:2 for reasons discussed in paragraph 5, supra, therefore the specification is not enabling for polynucleotides encoding variants of SEQ ID NO:2. If applicant were able to

overcome the 112, first paragraph rejection on SEQ ID NO:2, the specification would only be enabling for SEQ ID NO:2. The specification fails to give any guidance on the correlation between the amino acid sequence and the function of the protein, therefore one of skill in the art would not know how to modify the amino acid sequence without adversely affecting the function of the hypothetical protein. The art teaches that the modification of a protein sequence is not a trivial matter. Proteins are folded 3-dimensional structures, the function and stability of which are directly related to a specific conformation (Mathews and Van Holde, Biochemistry, 1996, pp. 165-171). In any given protein, amino acids distant from one another in the primary sequence may be closely located in the folded, 3-dimensional structure (Mathews and Van Holde, Biochemistry, 1996, pp. 166, figure 6.1). The specific conformation of a protein results from non-covalent interactions between amino acids, beyond what is dictated by the primary amino acid sequence. Thus, the resulting consequence of any given amino acid change is dependent upon what is substituted for the original amino acid and the three dimensional structural environment in which the given amino acid is located (Matthews, B. "Genetic and Structural Analysis of the Protein Stability Problem"). Often, when altering the amino acid sequence of a protein, a second alteration is necessary to restore the function of the protein. For example in hemoglobin, a mutation of Asp to Asn at position beta 99 results in a abnormal hemoglobin. In normal hemoglobin the Asp at position beta 99 is stabilized by a Try at position alpha 42 and an Asn at position alpha 97. The normal function of the mutated hemoglobin can be restored by producing a double mutant retaining the first mutation of Asn at position 99 beta in addition to substituting a Asp for Tyr at position alpha 42 (Kim et al, PNAS, 1994). As another example of the interactions of amino acids in a 3-dimensional protein structure, Frisch et al (Biol. Chem., Hoppe-Seyler, 1994, 375:353-356) observed that a human Vk protein of an antibody is destabilized after a substitution of Cys 23 . This de-stabilization was found to be reversed by a substitution of Try for His at position 32. Frisch concluded that there was a stabilizing interaction (non-covalent interaction) between the Cys 23 and the Tyr 32 in the original antibody. Thus it can

be conceived that compensatory changes throughout a primary amino acid sequence can result in a protein having the same shape and function as the original sequence. Additionally, Bork (Genome Research, 2000,Vol. 10, pp. 398-400) teaches that protein function is context dependent, and cellular as well as molecular aspects have to be considered (p. 398, col 2). However, given the lack of guidance in the specification for choosing which amino acids to exchange, either separately or in groups, and which specific amino acids can be substituted in at any specified location, one of skill in the art would not know how to make or use the instant invention.

(D)As drawn to polynucleotide variants of SEQ ID NO:1 and polynucleotides which hybridize to SEQ ID NO:1.

Claims 77 and 78 are drawn to polynucleotides which are 95% identical to SEQ ID NO:1 and polynucleotides which hybridize under stringent conditions to SEQ ID NO:1. Neither term is limiting with respect to the function of the claimed polynucleotides. Given the broadest reasonable interpretation, claims 77 and 78 encompass a substantial number of polynucleotides which would not share either structural or functional properties with the polynucleotide of SEQ ID NO:1 or encode proteins that share the putative properties of hypothetical SEQ ID NO:2. The specification fails to provide an enabling disclosure for how one would use such polynucleotides. The specification provides insufficient guidance with regard to these issues and provides no working examples which would provide guidance to one skilled in the art on how to use the broadly claimed species. For the above reasons, undue experimentation would be required to practice the claimed invention.

9. Claim 71 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 71 recites "a first nucleic acid". It is unclear what the applicant intends the second nucleic acid to be.

10. Claims 71 and 76 appear to claim the same invention. Appropriate correction is required.

11. All other rejections and objections recited in Paper No. 16 are withdrawn.

Conclusion

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Canella whose telephone number is (703) 308-8362. The examiner can normally be reached on Monday through Friday from 8:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

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Patent Examiner, Group 1642
November 20, 2000

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